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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/003,574	01/06/98	TRIPP C	2618-21-1-C1

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EXAMINER	
SCHNIZER,H	
ART UNIT	**PAPER NUMBER**
1653	9

DATE MAILED: 09/23/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

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Office Action Summary

Application No.	Applicant(s)
09/003,574	Tripp et al.
Examiner	**Group Art Unit**
Holly Schnizer	1653

☒ Responsive to communication(s) filed on *Jun 29, 1999*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1, 8, 11-13, and 15-25* is/are pending in the application.

Of the above, claim(s) *20-24* is/are withdrawn from consideration.

☒ Claim(s) *8* is/are allowed.

☒ Claim(s) *1, 11-13, 15-19, and 25* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *8*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1653.

Election/Restriction

2. Applicants' traversal of the restriction between Groups I-IV is acknowledged. The traversal is on the grounds that a search for the proteins of Group I is sufficient for the methods of Groups III and IV which use the product of Group I and that the antibodies of Group II are molecules specifically defined by its relation to the protein of Group I. The arguments with respect to the methods of Group III and IV are not persuasive because, as previously explained in Paper No. 6 mailed March 24, 1999, the inventions of Groups I and III and IV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the products as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using the product (M.P.E.P. §806.05(h)). In the instant case, the metalloendopeptidase of Group I can be used for its proteolytic activity which is a materially different process from the Group III process of animal treatment and the Group IV process of identifying inhibitors.

3. Thus while Groups I, III, and IV are related, the Examiner has properly applied the standards for restricting between them. As for the assertion of no undue search or examination,

the Examiner has previously explained (in the Paper noted above) that the groups have a separate status in the art. Therefore, search of Groups III and IV includes class 424, subclass 4 which is not co-extensive with the searches required for Group I (class 435, subclass 212) and would thus constitute a serious burden upon the examiner if combined.

4. With respect to Groups I and II, the Examiner has considered Applicants arguments and will rejoin the antibody of Group II with the protein of Group I. Applicants argued that the antibody of Group II is a molecule specifically defined by its relation to the protein of Group I and cite *In re Gold*, 42 USPQ2d 1095 (Comm'r Pats., unpublished), to support their contention that the patentable distinctness between the claimed antibody of Group II and the protein of Group I is sufficiently close to warrant the withdrawal of the restriction requirement. Since *In re Gold* also states that a restriction should not be required if there is express admission that the claimed inventions are obvious over each other within the meaning of 35 U.S.C. 103, the Examiner interprets Applicants argument as an express admission that the antibody of Group II is obvious over the protein of Group I and thus if the protein of Group I is anticipated or obvious then the antibody of Group II would also be obvious.

5. The restriction requirement is deemed proper and therefore made FINAL.

Status of the Claims

6. The amendments filed on June 15, 1999 (Paper No. 9) and the supplemental amendment filed June 29, 1999 have been entered. Claims 2-7, 9, 10, and 14 have been canceled and Claim

25 has been added (and amended). Therefore, Claims 1, 8, 11-13, 15-25 are pending. Claims 20-24 are withdrawn as directed to a non-elected invention.

Rejections Withdrawn

7. The rejection of Claims 10, 14, and 19 as indefinite under 35 U.S.C. 112, 2nd paragraph, has been withdrawn in light of the cancellation of Claims 10 and 14 and the amendment of Claim 19.

8. In light of the cancellation of Claims 2-7, 9, 10, and 14 and upon reconsideration, the rejection of Claims 1-7. 9, 12-14, and 16-19 under 35 U.S.C. 112, first paragraph for lack of written description has been withdrawn. Astacin metalloendopeptidases are known in the art and Applicant has provided the polynucleotide sequence of several metalloendopeptidases isolated from *D. immitis* (SEQ ID NOS: 3-11, 31 and 34).

9. The rejection of Claims 1,2, 9-10, 12, 14-16, 18, 20-21, and 30 under 35 U.S.C. 112, first paragraph for lack of enablement is withdrawn. Applicants have canceled Claims 2-7, 9, 10 and 14 therefore rendering the rejection of these claims moot. Applicants argued that the amount of experimentation required to identify proteins in the present application is not undue and that it would be known by one of skill in the art how to identify additional proteins using the specified nucleic acid molecules and proteins of the present invention. In addition, Applicant directs attention to the examples which describe the presence of the nucleic acid molecules in D. immitis (example 1), use of D. immitis DNA to isolate additional nucleic acid molecules and identify Astacin metalloendopeptidase encoding nucleic acids (example 2); and incorporation of the

nucleic acid molecules and cells in order to produce Astacin metalloendopeptidase proteins of the present invention(examples 3-5). In light of Applicants examples and the fact that Astacin metalloendopeptidases are well known in the art the Examiner finds Applicants arguments persuasive and withdraws the rejection.

New Rejections

Claim Rejections - 35 USC § 112

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 1, 11-13, 16-19, and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

12. The recitation of "hybridizes under stringent conditions" renders Claims 1, 11-13, and 16-19 indefinite. Applicants have not sufficiently defined the conditions under which hybridizations are to take place. Nucleic acid hybridization is extremely sensitive to the conditions in which it is performed and the definition of stringency as it pertains to hybridization conditions is subject to different interpretations from laboratory to laboratory. The buffer composition, pH, temperature, length of time, salt concentrations, quality and source of template nucleic acid are all variables which determine the reproducibility of a given hybridization experiment. The specification refers to Molecular Cloning: A Laboratory Manual (page 16) for teachings of stringent hybridization

condition, but this reference is a non-limiting example, not a definition. Without a clear and explicit recitation of the conditions which are encompassed by the claimed invention, Claims 1, 11, and 16 are indefinite. Claims 12, 13, and 17-19 are rejected since they depend from indefinite claims. This rejection can be overcome by including defined hybridization conditions in the claim.

13. Claim 25 is indefinite for the recitation of "about 9 contiguous amino acid region". An amino acid is a definite measure and the specification fails to define how many amino acids are encompassed by the term "about" therefore, the metes and bounds of the claims are unclear.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15. Claims 1, 11-13, 16, 18, and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Dumermuth et al (J. Biol. Chem. (1991) 266(32): 21381-21385; reference 5 of IDS filed March 13, 1998).

16. Applicants disclose that Astacin metalloendopeptidases have been found in a wide variety of sources such as human, mice, rats, *Drosophila*, *Xenopus* frogs, and sea urchins (see pages 4-5) and refer to Dumermuth et al. for support. In addition, to characterizing the sequence similarity of the family of Astacin metalloendopeptidases, Dumermuth et al. teach the cloning of a human

intestinal brush border metalloendopeptidase and a mouse kidney brush border metalloendopeptidase both of which have strong similarities to Astacin metalloendopeptidase.

17. The Claims of the present invention are drawn to any protein encoded by any nucleic acid molecule that hybridizes under "stringent conditions' with the sequences defined in the claim and which elicits an immune response against a protein having one of the amino acid sequences defined in the claim. Since is unclear as to what conditions are intended as "stringent", and the polynucleotides disclosed in the Dumermuth et al. reference are from the same family as the claimed polynucleotides, the reference meets this limitation of the claims because the appropriate hybridization conditions would allow hybridization of the polynucleotides disclosed in Dumermuth et al. with the claimed polynucleotides. Moreover, Dumermuth et al. teach that the proteins of the family of Astacin metalloendopeptidases are highly homologous in sequence and all contain the extended sequence motif (the zinc binding domain) HEXXHXXGFXHE (page 21385, column 2, lines 5-6) thus, these disclosed proteins comprise "at least a portion of" the claimed amino acid sequences of Claim 11. Furthermore, Dumermuth et al. provide a hydropathy analysis (page, figure 3) to demonstrate sequence and structural similarity between members of the Astacin family and suggest that several cysteines, completely conserved among Astacin family members, are likely to be involved in maintenance of the conserved overall tertiary structure (page 5, column 12, paragraph 2). Since the claimed proteins are members of the Astacin family which are very similar in sequence and structure, it would be expected that proteins disclosed in Dumermuth et al. reference would elicit an immune response to the proteins having the amino acid sequences defined in Claims 1, 11-12, and 16

18. Claim 13 is a product by process claim. If a product in the product-by-process claim is the same as a product of the prior art, the claim is unpatentable even though the prior product was made by a different process (see MPEP 2113). Thus, for the same reasons a cited above, the Dumermuth et al. reference meets the limitations of Claim 13.

19. Claims 18 and 19 only differ from Claim 16 in that they limit the intended use of the claimed composition. The recitation of "for protecting an animal from disease caused by a parasite" has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the structural limitations are able to stand alone. (MPEP 2111.02). Therefore, the Dumermuth et al. reference meets the limitations of Claims 18 and 19 for the same reasons stated above with respect to Claim 16.

20. The Examiner notes that including the limitation that the protein is from *D. immitis* and including specific hybridization conditions with a percentage nucleic acid sequence identity of the nucleic acid molecules that would hybridize under such conditions would serve to overcome this prior art rejection of Claims 1, 13, and 16-19. With respect to Claim 11, overcoming this prior art rejection would also require deletion of the phrase "at least a portion" since the reference discloses at least a portion of the amino acid sequence identical to the claimed amino acids sequences.

21. Claim 25 is rejected under 35 U.S.C. 102(b) as being anticipated by Waterston, (1995) Accession No. U41554 to EMBL/GenBank/DDBJ Data Banks).

22. Waterston discloses an amino acid sequence of a zinc protease having several regions with amino acids which are 100% identical to amino acids of SEQ ID NOS: 31 and 34 (see sequence alignment attached to this office action). In particular, a region at position 280-292 has a region of 13 amino acids which are 100% identical to the sequences of SEQ ID NO: 31 and 34. Thus, the Waterston sequence meets the limitations of Claim 25 since it is a homolog of the claimed proteins and has at least about 9 contiguous amino acids identical in sequence to a 9 contiguous amino acid region of the amino acid sequence of SEQ ID NO: 31 and 34.

Claim Rejections - 35 USC § 103

23. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

24. Claims 1, 11-13, 15-16, 18, and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dumermuth et al. as applied to claims 1, 11-13, 15, 18, and 19 above, and further in view of applicants admission.

25. The teachings of Dumermuth have been described in paragraph 17 of this office action render Claims 1, 11-13, 16, 18, and 19 obvious for the reasons stated above. Claim 15 is directed to an antibody capable of selectively binding to the protein of Claim 1. As explained in paragraph

4 of this office action, Applicants contention that the patentable distinctness of the claimed antibody and protein is sufficiently close to warrant withdrawal of the restriction requirement between them has been interpreted as an express admission that the claimed inventions are obvious over each other within the meaning of 35 U.S.C. 103. Thus since the claimed protein of is anticipated and obvious over Dumermuth et al. then the antibody is also obvious because it is obvious to make an antibody to any known peptide.

Allowable Subject Matter

26. A thorough search of the prior art and of the sequence databases did not find any proteins with sequences identical to the sequences defined in the claims or a protein comprising a *D. immitis* Astacin metalloendopeptidase. Therefore, Claim 8 is allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Holly Schnizer whose telephone number is (703) 305-3722. The examiner can normally be reached Monday-Friday from 7:30 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bradley Sisson, can be reached at (703) 308-3978. The fax phone number for Official Papers to this Group is (703) 308-4242. Any inquiry of a general nature or relating to the status

of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Holly Schnizer, Ph.D.
September 22, 1999

Karen Cochrane Carlson PhD

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER